EXHIBIT 6

Cephalon
deliver more

Cephalon, Inc.
41 Moores Road
P.O. Box 4011
Frazer, PA 19355
Phone: 610-344-0600
Fax: 610-344-0065

March 29, 2007

Dr. Robert Rappaport, Director
Division of Anesthesia, Analgesia,
and Rheumatology Products, HFD-170
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 20-747
Actiq® (oral transmucosal fentanyl citrate, OTFC®)
Risk Management Program –31st. Quarterly Report

Dear Dr. Rappaport:

Reference is made to Section 10 of the most currently approved Risk Management Program (RMP) approved on February 19, 2003 (Supplement No. S-008), in which we commit to provide a quarterly report with the information specified in the RMP. This correspondence contains the RMP 31st. quarterly report. Per the Agency's request on August 23, 2005, we are providing six additional desk copies.

If you have any questions regarding this submission, please contact me at 610 738-6237 or via email to cmarchio@cephalon.com.

Sincerely,

Carol S. Marchione

Carol S. Marchione
Senior Director and Group Leader
Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Cephalon,Inc.	March 29, 2007
TELEPHONE NO. *(Include Area Code)*	FACSIMILE *(FAX)* Number *(Include Area Code)*
(610) 344-0200	(610) 738-6642
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):* 41 Moores Road, P.O. Box 4011, Frazer, PA 19355	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 20-747

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY	
oral transmucosal fentanyl citrate, OTFC	Actiq	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*		CODE NAME *(if any)*
N-(1-phenethyl-4-piperidyl) propionanilide citrate (1:1)		
DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Solid, compressed matrix	200, 400, 600, 800, 1200, 1600 ug	oral transmucosal

(PROPOSED) INDICATION(S) FOR USE:

Actiq is indicated only for the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for their underlying persistant cancer pain.

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) ☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug _____ Holder of Approved Application _____

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO APENDING APPLICATION ☐ RESUBMISSION ☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION

31st Quarterly RMP Report

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Information previously provided and can be made available upon request.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

DMF 10128: Fentanyl Citrate
DMF 13048: Holder/Handle Resin
DMF 819: Artificial Berry Flavor
DMF 7273: Blister Peel-Push Lidding
DMF 3764: Blister Roll Stock
IND 27, 428 Oral Transmucosal Fentanly (OTFC)
NDA 20-195 Fentanyl Oralet (Oral Transmucosal Fentanyl Citrate) 100, 200, 300, 400 ug fentanyl base

This application contains the following items: *(Check all that apply)*

☐	1. Index
☐	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☒	20. OTHER *(Specify)* 31st Quarterly RMP Report

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
Carol S. Marchione	Carol S. Marchione Senior Director and Group Leader, Regulatory Affairs	March 29, 2007

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
41 Moores Road, P.O. Box 4011 Frazer, PA 19355	(610) 344-0200

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Actiq® Risk Management Program

31st Quarterly Report
(October 1, 2006 through December 31, 2006)

Actiq Surveillance and Monitoring Program (Sections 8.0 and 9.0)

8.0 Surveillance Goals and Activities

8.1 Direct Patient Feedback

8.1.1 Chain Pharmacy Call Back System

Since the implementation of the Risk Management Program for Actiq through December 31st, 2006 Cephalon, Inc. has received cumulative data from 18,118 patient interviews conducted by Walgreens, CVS Procare and Eckerd Drugs. Due to logistical reasons, however, only Walgreens Pharmacy is currently participating. Accordingly, the number of call-backs conducted by Walgreens has increased. The geographic distribution of the patients surveyed includes individuals from most of the contiguous United States.

Quarterly results from the completed patient surveys are summarized in Appendix 1. Of the 2,312 unique patients identified by Walgreens as being eligible for the survey this quarter, (i.e. patients filling their *initial* Actiq prescription at a Walgreens pharmacy), 612 were successfully contacted and surveyed. This represents a 27% response rate for the period, which is a full 10 percentage points lower than last quarter's 37% (814/2,198), and well below the 45% average (2,551/5,698) for the last three quarters of 2005.

It should be noted that during this reporting period, two generic oral transmucosal products were introduced to the market. The Walgreen's survey data presented for 4th quarter 2006 (01-October-2006 through 31-December-2006) does not include data from patients who filled an initial prescription for generic OTFC. These patients will be included in the pharmacy callback program beginning late first quarter 2007.

The survey itself primarily addresses three key components of the Actiq RMP: proper storage and disposal of Actiq units, opioid tolerance status of the patient, and preventative measures to mitigate risk of pediatric exposure. Quarterly survey findings (based on the percentage of total respondents) for the three key components of the RMP revealed that of the 612† patients surveyed, there were 274 responses to the question regarding receipt of the Welcome kit. Approximately 57% (156/274) of the responses indicated that the patient had received an Actiq Welcome Kit with their prescription compared with approximately 21% (92/440) in third quarter 2006. It should be noted that approximately 338, or 55% (338/612) of survey participants were not asked if they received a Welcome Kit with their prescription. This occurred when the pharmacists conducting the survey became aware that the Welcome Kits were out-of-stock so they elected to not ask the survey question pertaining to the Welcome Kits. Cephalon was not initially informed of the situation. Thus, fewer kits were distributed by Walgreens during this reporting period.

Cephalon became aware of the omission of this question from the patient interview upon receipt of the completed survey forms for October 2006 and requested that the survey be administered as designed. Thus, the e 4th quarter patient survey data should not be viewed as representative of the overall distribution of Welcome Kits. A training session is being

scheduled for the pharmacists conducting the survey to emphasize the importance of consistent survey techniques and to increase their knowledge of the Actiq Risk Management Program.

The results of the survey showed:

- The majority (85%; 506/597; 15 N/A) of patients reported that their pharmacist or physician instructed them about proper storage and usage of Actiq.

- The overwhelming majority (97%; 585/606; 6 N/A) of patients were opioid tolerant *prior* to starting Actiq therapy. This is fairly consistent with cumulative data received to date from survey respondents.

- Concerning children with access to the home, nearly 43% (256/602; 10 N/A) of patients surveyed during the quarter reported children lived in or had access to their homes. When asked where *unused* Actiq units are *stored*, the majority of responses indicated that either a locked cabinet (44%) or some other type of storage container (21%) was utilized. However, because patients may report several modes of storage, it is not possible to determine the primary mode of storage in these instances. Seven percent of the responses indicated the Welcome Kit was used for this purpose.

- The overwhelming majority of responses (77%; 539/703) indicate the trash bin is utilized for *disposal* of *finished units*. Only four percent (31/703) of the responses indicated use of the Welcome Kit for disposal purposes.

- Regarding the *disposal* of *partially used (unfinished)* units, approximately 27% (243/914) of responses indicated the Actiq units were always finished prior to disposal. It is noted that this is a significant decrease from the 2006 YTD percentage totals (27% vs. 48%) and although higher than the cumulative total of 18%, it is not possible to determine the reason for this decrease using the current survey questions.

[†] All values given are approximates rounded to the nearest whole number.
N/A = question not answered

In addition to direct patient feedback obtained through the Pharmacy Call-Back program, Cephalon, Inc. requests information regarding Welcome Kit usage from all *Actiq* users who call the Company's 1-800# to request patient assistance, report adverse events or product complaints. Data obtained during this quarter revealed that 35% (183/528) of the callers indicated they had a Welcome Kit, representing a 16% increase from the prior quarter (35% vs. 19%). Of the 183 patients who had a Welcome Kit, 56% (103/183) indicated they currently used it.

8.2 Prescription Monitoring

8.2.1 NDC Source Prescriber Audit

Data from the NDC Source Prescriber audit show that none of the non-targeted physician specialties exceeded 15% of total prescriptions during 4Q06.

8.2.2 IMS National Disease and Therapeutic Index (NDTI)

Data from the IMS National Disease and Therapeutic Audit (NDTI) showing the use of Actiq during the 4th. Quarter 2006 are shown in Appendix 2.

8.2.3 Wholesaler Data

Quarterly wholesaler to retail shipment data for the 4th. Quarter 2006 has been forwarded to the sales representatives for follow-up during their regular field.

8.3 Adverse Drug Reactions (ADRs)

8.3.1 Cephalon Standard Operating Procedure

Cephalon, Inc. has established procedures to guide processing of all adverse drug reaction reports. Any adverse drug reaction, as defined by current federal regulations, receives immediate evaluation and follow-up as defined in Cephalon's Standard Operating Procedures.

A toll-free number that may be accessed 24 hours a day is available to receive adverse drug reaction reports. Reports are logged into the Global Product Safety database, regardless of source, and processed according to Cephalon's procedures and guidelines. Global Product Safety is responsible for the processing of adverse drug reaction reports and for briefing senior management as appropriate.

The processing of ADR reports is guided by a Standard Operating Procedure summarized below.

(a) Each ADR report is reviewed to confirm the initial report classification, the reported ADR term, and to assess the report for seriousness, relatedness, and expectedness, based on criteria outlined in 21CFR314.80. In addition, for reports associated with Actiq, these findings are then reviewed to determine reportability in accordance with the Special Safety Commitments for Actiq (see Section 8.3.2).

(b) The reporter is contacted by Global Product Safety in a timely fashion should additional information be required.

8.3.2 Special Safety Commitments

In addition to the requirements for 15-Day Safety Alerts under 21CFR314.80, the RMP requires that the following events received from US spontaneous sources be reported in an expedited fashion:

- **Any unintended pediatric exposure**, whether or not serious and whether or not unexpected

- **Any serious adverse drug reaction (SAE)** which is determined to occur in the **context of diversion** (i.e., use by an individual other than for whom it was prescribed), whether or not considered unexpected

- **Any serious adverse drug reaction (SAE)** which is determined to occur in the **context of "off-label use"** (i.e., used outside of the approved indication for Actiq) whether or not considered unexpected.

The following table (Table I) summarizes all reports meeting the Actiq RMP criteria received during this reporting period for Actiq, including reports that meet the criteria outlined in the Special Safety Commitments for Actiq. Spontaneous data received for the two generic OTFC products is reflected in the aggregate data presented in Table I.

Table I. *Actiq* Product Experience Reports[1]
Quarter ending 31 December 2006

Month, 2006	Total No. of RMP Cases‡	Off-Label Prescribing[A]	SAE Related to Off-Label/ On-Label§ Use	Unintended Pediatric Exposure	Diversion* SAE/No SAE
October	267	73** 58*** 128****	2/0	0	0/5
November	159	46** 34*** 74****	1/0	2	0/5
December	101	25** 22*** 52****	1/0	0	1/1

[1]See Appendix 3 for a cumulative tabulation of cases to date. Table excludes non-serious, on-label SAEs and foreign (ex-U.S.) cases that may represent off-label use.

‡ **Total number of cases includes off-label prescribing, pediatric exposures, and diversion. Excludes SAEs from on-label use.**

* Column does not include 7 reports of possible diversion.
** Appropriate physician follow-up letter scheduled or sent.
*** Physician's name was incomplete or not revealed; therefore, follow-up letter could not be sent.
**** Repeat incident notification scheduled or sent.
§ On-label use includes reports where indication is unknown.

A total of 527 reports meeting RMP criteria were registered in October, November and December 2006. The majority of the reports (512/527; 97%) represented instances of off-label prescribing. Of the 527 cases, 398 had sufficient information to contact the prescriber regarding proper use (i.e., 144 initial letters and 254 repeat incident notifications).

Two of the 527 (<1%) cases received during this reporting period involved an unintended pediatric exposure to Actiq. There were 5 SAEs associated with off-label use and 1 SAE associated with diversion during the quarter. Thus, a total of 8 cases were determined to meet the Actiq RMP reporting criteria as 15-Day Alerts during the reporting period (see Table II).

Table II. *Actiq* Reports Submitted as 15-day Alerts under the RMP Quarter Ending 31 December 2006

Report Type	Cephalon MCN	Submission Date
Initial Reports:		
SAE Related to Off-Label Use	**US012207**	**18-Dec-2006**
	US018378	**12-Oct-2006**
	US018425	**18-Oct-2006 (initial)** **11-Jan-2007 (follow-up)**
	US018763	**08-Nov-2006**
	US018778	**15-Nov-2006 (initial)** **22-Dec-2006 (follow-up)**
SAE Related to Diversion	**US019154**	**12-Jan-2007**
Unintended Pediatric Exposures	**US018789**	**16-Nov-2006 (initial)** **22-Dec-2006 (follow-up)**
	US018796	**22-Dec-2006**

Actiq reports received during the reporting period and expedited under the RMP are summarized by reporting category below.

ADRs Expedited under the Actiq Risk Management Program

Unintended Pediatric Exposures

During this reporting period, there were 2 new reports of unintended pediatric exposure. These cases are described below:

US018789: Report received from a newspaper article that reported an in-utero exposure to Actiq and perinatal complications. The infant was born on 25-October-2002 to a mother with a previous history of narcotic addition who developed an addiction to Actiq (see Reports of off-label use –US018778). The infant was also exposed in-utero to Norco (acetaminophen/hydrocodone) and heroin until two weeks prior to birth. The infant was described as pink, screaming, and healthy. However, the infant remained hospitalized for

~five weeks for observation and treatment of withdrawal symptoms. There were no reported lingering effects from the in-utero opioid exposure.

US018796: Report received from a consumer regarding a 2-year-old male who was exposed to an Actiq lozenge, 800mcg. The child picked up an Actiq lozenge which had been lying on his grandmother's bed in the blister packaging and placed it into his mouth. It was not known if the blister package was open at prior to the child's exposure. It was reported that total exposure to the lozenge was only a few seconds before the grandmother retrieved the lozenge. The child had no adverse effects.

Comment: Prior to this exposure, it was reported that the grandmother did not have a Welcome Kit. However, the grandmother reported that she had tried to obtain a kit in the past. A kit was requested for her at the time of the report to Cephalon.

Serious ADRs Associated with Off-Label Use

Currently, Actiq is indicated for management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for underlying persistent cancer pain. There were five cases (US012207, US018378, US018425, US018763, US018778) involving a serious ADR reported in the context of off-label use received during the reporting period. The cases are listed below in Table III.

Table III. Serious ADRs Associated with Off-Label Use

Cephalon Case Number	Age/Gender	Treatment indication	Reported ADR	Outcome	Note
US012207 – Important Medical Event	53/F	Chronic back pain	Dental decay; bacterial infection	Not recovered	Patient required extensive dental treatment and surgery
US018378	34/F	Back pain	Drug withdrawal, nausea and vomiting	Recovered from nausea and vomiting. Mild withdrawal symptoms persist.	Hospitalized twice for severe nausea and vomiting.
US018425 – Important Medical Event	43/F	Migraine pain	Overdose, unresponsive to stimuli, oxygen saturation decreased (O^2 sat 30%)	Recovered (required treatment with Narcan)	At the time of the event, the patient was in a psychiatric facility. Patient had a history of prior adverse reactions to narcotics, fibromyalgia and concurrent psychiatric illness
US018763	60/M	Chronic back pain and neuropathy	Drug withdrawal syndrome, diarrhea	Recovered	Abrupt discontinuation of opioid therapy. Required hospitalization. Concomitant therapy included oxycontin.
US018778	23/F	Migraine pain	Drug dependence	Recovered – required detoxification treatment	Mother of infant cited in US018789. History of prior narcotic addiction. Also abused heroin, hydrocodone.

Serious ADRs Associated with Diversion

There was one report of a serious ADR reported in association with a possible diversion of Actiq.

US019154: This report was identified in a newspaper article reporting the death of a college student. The student was a 20 year-old male whose death was attributed to a mixture of fentanyl, cocaine, and alcohol. The source and formulation of the fentanyl is unknown. The medical examiner noted that cocaine was found in the decedent's room. It was also reported that the student had not been prescribed fentanyl and had apparently obtained it illicitly. The cause of death was reported as toxic effects from cocaine, ethanol and fentanyl.

8.3.3 Literature Monitoring

No serious adverse events were received during the reporting period from published scientific literature sources.

8.4 Poisoning and Overdose

This section summarizes all Poison Control Center reports received via either Cephalon's toll-free number monitored by Rocky Mountain Poison and Drug Center (RMPDC) or the Toxic Exposure Surveillance System (TESS). TESS data includes exposure reports received from over 60 U.S. Poison Control Centers (see program description in Section 8.4.2).

8.4.1 Central 1-800 Poison Control Number (RMPDC)

8.4.1.1 Poison Control Telephone Reports

This section summarizes reports received via Cephalon's toll-free Poison Control Center number. The table below includes all calls of a poison control or adverse drug reaction nature. As part of our contractual agreement with RMPDC, we have incorporated questions regarding the use and availability of the Welcome Kit in the RMPDC operating protocol for the Actiq RMP program.

There were three Actiq calls received at the Rocky Mountain Poison and Drug Center during this reporting period. All involved non-serious ADRs (see Table IV.)

Table IV. Reports Received via Cephalon's toll-free number (RMPDC)

Date of Report	RMPDC Case #	Cephalon ADR Case #	State	Type of Report
14-October-2006	1576990	US018527	CA	Report of intentional drug misuse involving 49-year-old female who experienced vomiting, dizziness/vertigo and malaise following consumption of a 1600mcg Actiq lozenge obtained from 'someone else' for pain relief. The patient's symptoms began one hour after ingesting the lozenge. The patient was instructed to call 911 and to seek treatment at an emergency room. The consumer was lost to follow-up, thus further information was not obtainable. Report assessed as non-serious ADR occurring in the context of diversion.
09-Nov-2006	1592718	US018856	LA	Non-serious ADR involving 57-year-old female who experienced mouth soreness related to Actiq use.
27-Dec-2006	1619274	US019108	NC	Non-serious ADR involving 20-year-old female who experienced dizziness and nausea after ingesting half of a 1600mcg lozenge that broke during use.

8.4.2 Toxic Exposure Surveillance System (TESS)

Toxic Exposure Surveillance System (TESS) data are compiled by the American Association of Poison Control Centers (AAPCC) in cooperation with the majority of US poison centers. The cumulative AAPCC database now contains approximately 41 million human poison exposure cases. This database is now referred to as the New Core System Beta National Poisoning and Exposure Database (NCSBeta).

There were no new TESS reports received during the reporting period. However, Cephalon received follow-up information regarding the six fatalities associated with use of fentanyl that were listed in the 2005 TESS Annual Report. The route of exposure was reported as ingestion. Of the six fatalities listed, one death was attributed to Actiq. This case was reported through Rocky Mountain Poison and Drug Center and was submitted as a 15-day report in 2005 (case # US015829).

8.5 Abuse and Diversion

Information regarding abuse and diversion of Actiq is derived from spontaneous ADR reports as well as a number of additional sources (see Section 8.5.1). Approximately 3.6 million Actiq units were dispensed during 4th quarter 2006 and there were a total of 19 reports of suspected diversion (includes 7 reports classified as possible; pending receipt of additional information) received during this period.

One of the 19 reports involved a suspected diversion of approximately 1,000 Actiq units. This report was identified in a newspaper report published in December 2006 in which it was reported that two employees of a physician's office were arrested on suspicion of prescription forgery[1]. This forgery involved approximately 1,000 Actiq units. Follow-up of this report was attempted, however, the law enforcement official advised that the investigation is ongoing, therefore no additional information was provided to the Company.

Another newspaper article contained a report regarding the abuse of Actiq as well as other prescription opioids and illicit drugs. This report (US018778) is described in Section 8.3.2 – Serious ADRs associated with off-label use.

8.5.1 State Drug Control Authorities or State Boards of Pharmacy

There were no contacts involving State Boards of Pharmacy. Drug control authority contacts included:

- DEA request for Actiq dummy units and educational information for training purposes.

- Company presentations to NASCSA (National Association of State Controlled Substance Authorities) and NADDI (National Association of Drug Diversion Investigators).

8.5.2 Drug Abuse Warning Network (DAWN)

The Drug Abuse Warning Network (DAWN) is a voluntary, national public health surveillance system that gathers information on substance abuse that results in visits to hospital emergency departments (EDs) and drug-related deaths reviewed by medical examiners and coroners. Data are currently being collected from a national probability sample of 260 non-Federal short stay hospitals in the coterminous United States. These data are used in combination with other information to identify emerging drug abuse problems.

In 2003, DAWN was redesigned to improve data quality and data content. Any ED visit related to recent drug use is considered a DAWN case for purposes of data collection,

[1] Trahan J, Hacker, H. Potent painkiller blamed in SMU student's death. The Dallas Morning News (Park Cities) 2006 Dec 20.

including substance abuse or intentional or accidental drug misuse. ED visits related to the use of drugs for legitimate therapeutic purposes are also included.

In addition to active review of DAWN publications, Cephalon, Inc. has been granted access to the DAWN Live! database which will enhance our surveillance and knowledge related to emergency department visits associated with misuse, abuse and accidental ingestion of Actiq. DAWN Live! data reflects the number of emergency department visits in the category of interest (e.g., non-medical use). It should be noted that this is raw data that may be incomplete and is not useful for trending. However, it may provide an early indication of potential product issues related to abuse, misuse (non-medical use) and other drug-related emergency department visits.

A query of the DAWN Live! database was performed on 29-January-2007 to obtain data related to misuse, abuse, and accidental ingestions involving Actiq.

Search strategy

- **Date range for query:** September 2006 to December 2006.
- **Sample size**: 282 Emergency Departments provided data out of the 1,021 EDs in the DAWN sample.
- **Drugs:**: The following drug names were searched to capture all reports that may represent an ED visit associated with use of Actiq: Fentanyl Citrate, Fentanyl Suckers, Fentanyl Lollipop, Fentanyl Pops, Actiq
- **Search Terms**: listed in Table V. below.

Table V. Number of DAWN Live! ED visits reported for Actiq from Sep–2006 to Dec-2006

Search Term(s) – case types	Sep 2006	Oct 2006	Nov 2006	Dec 2006
Accidental Ingestion	0	0	0	0
Overmedication, malicious poisoning, other**	2 (Actiq)	0	0	0

Search date: 29-Jan-2007 5:43 PM – 6:04 PM; except as otherwise noted.
** Search date: 1/26/2007 5:22 PM (279 EDs in sample). Non-medical use is categorized using a grouping of the case types shown in the above table. The 'Other' category may include illicit drugs, toxicity and withdrawal.

Results: There were two emergency department visits related to non-medical use of Actiq. The patients (1 male, 1 female) were evaluated in an ER in September 2006 following exposure to Actiq. Both patients were age 45 – 54 years of age. No information was provided regarding the patients' diagnoses. It was reported that one patient was discharged and the other patient was admitted to a psychiatric unit.

8.6 Promotional Message Audit

As of September 25, 2006, Cephalon ceased all promotion and sales force activity associated with Actiq. Since the promotional message audits were designed specifically to monitor these activities, we have cease to conduct this audit and reporting activity. In our response to S-020 regarding revision to the RMP, which is in the process of being reviewed by the Agency, we have proposed to delete this activity from the program. A response from the Agency is pending.

9.0 Intervention

9.1 Off-Label Usage

9.1.1 Individual Prescribers

When reports containing any mention of off-label usage of Actiq are received and where the prescriber contact information is known, the following procedures are followed:

1) First instance of off-label use: A letter from Global Product Safety is mailed to the prescriber emphasizing the approved indication, appropriate patient selection, and key safety messages. An electronic copy of the letter is stored in the Global Product Safety electronic files.

   Instances of off-label use are detected via Cephalon's standard surveillance processes (i.e., ADR reporting, product complaint reporting, medical information inquiries).

   During this reporting period, 144 off-label letters were sent to prescribers identified as prescribing Actiq for off-label use.

2) Prescribing patterns will be monitored for repeat instances by the same prescriber.

   During the reporting period, 254 repeat instances of off-label prescribing were identified. For each of these instances, an email notification was sent to Cephalon's Sales and Marketing Department containing the contact information for all prescribers identified as repeat prescribers.

9.1.2 Groups of Prescribers

Data from the NDC Source Prescriber audit as per Section 8.2.1 show that none of the nontargeted physician specialties exceeded 15% of total prescriptions during 4Q06.

9.2 Unintended Pediatric Ingestion

All reports received regarding an unintended (accidental) pediatric ingestion are processed as expedited ADRs under our special safety commitment. There were a total of 2 unintended pediatric exposures this quarter (includes one in utero exposure); both cases are described in Section 8.3.2.

Appendix 1

8.1.1 Chain Pharmacy Call Back System

Under this program, patients who receive an Actiq prescription at a participating Walgreens pharmacy will receive a follow-up phone call by a company pharmacist. It should be noted that with each survey the patient and/or caregiver is reminded that:

- Actiq is only for breakthrough cancer pain for those patients who are taking chronic opioids.
- Actiq must be kept in a locked space where children do not have access.
- The items in the Actiq Welcome Kit should be used to protect children in the home.
- A toll-free number (888-818-4113) is available for patient questions and to request a Welcome Kit.

As of **December 31st, 2006**, Cephalon Inc. has received cumulative data from 18,118 patient interviews. A review of the data revealed that some survey records were entered without call dates. Due to the query design used to generate the quarterly summary, these records were not included in the RMP tabulations prior to the 20th quarterly report. These records have since been added to the summary tables.

Statistics from the Quarterly (31st), YTD (2006) and Cumulative (since April, 2000) survey results are summarized below. Because in some questions (i.e., #5, 7 & 8) more than one response may be given and recorded, the total responses for these questions may be greater than the cumulative total of respondents surveyed. Answers not provided have been labeled "N/A", although not all of these particular responses have been accurately accounted for in the database. This explains the discrepancy in the totals reported for Question #5 below vs. the *cumulative* total of all cases received to date (i.e. 17,315 vs. 18,118).

Comparative Results

Data Point	Qtr 4	YTD Totals 2006	Cumulative Totals: *(Through Inception)*
Unique Patients	2,312	9,086	NA
Surveys Conducted	612	2,583	18,118
Welcome Kits Distributed from Walgreens Pharmacy:	80	784	NA
October	0		
November	48		
December	32		

Question (1):
"Rcvd Actiq Welcome Kit with Rx?"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 274)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 1,870)*	**Totals**	**% Of Total** *(n =18,118)*	**% Of Respondents** *(n = 17,047)*
Yes	156	25.5%	56.9%	367	14.2%	19.6%	3,690	20.4%	21.6%
No	118	19.3%	43.1%	1503	58.2%	80.4%	13,357	73.7%	78.4%
N/A	338	55.2%		713	27.6%		1,071	5.9%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

Question (2):
"Already on an opioid prior to Actiq Rx?"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 606)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 2,573)*	**Totals**	**% Of Total** *(n =18,118)*	**% Of Respondents** *(n =17,633)*
Yes	585	95.6%	96.5%	2520	97.6%	97.9%	16,667	92.0%	94.5%
No	21	3.4%	3.5%	53	2.1%	2.1%	966	5.3%	5.5%
N/A	6	1.0%		10	0.4%		485	2.7%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

Question (4):
"Advised about proper Actiq storage and usage?"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 597)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 2,543)*	**Totals**	**% Of Total** *(n = 18,118)*	**% Of Respondents** *(n = 17,202)*
Yes	506	82.7%	84.8%	2285	88.5%	89.9%	15,189	83.8%	88.3%
No	91	14.9%	15.2%	258	10.0%	10.1%	2,013	11.1%	11.7%
N/A	15	2.5%		40	1.5%		916	5.1%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

Question (5):
"Where do you store your unused Actiq units?"**

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 639)*	**% Of Responses** *(n = 639)*	**Totals**	**% Of Total** *(n = 2,625)*	**% Of Responses** *(n = 2,625)*	**Totals**	**% Of Total** *(n = 17,315)*	**% Of Responses** *(n = 17,315)*
Welcome Kit	47	7.4%	7.4%	110	4.2%	4.2%	310	1.8%	1.8%
Medicine Cabinet	49	7.7%	7.7%	534	20.3%	20.3%	4,038	23.3%	23.3%
Locked Cabinet	281	44.0%	44.0%	686	26.1%	26.1%	5,194	30.0%	30.0%
Leave in box - No special storage	126	19.7%	19.7%	782	29.8%	29.8%	2,827	16.3%	16.3%
Other	136	21.3%	21.3%	513	19.5%	19.5%	4,946	28.6%	28.6%
Totals:	639	100.0%	100.0%	2,625	100.0%	100.0%	17,315	100.0%	100.0%

Question (6):
"Children visitors?"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 602)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 2,564)*	**Totals**	**% Of Total** *(n = 18,118)*	**% Of Respondents** *(n = 16,726)*
Yes	256	41.8%	42.5%	672	26.0%	26.2%	5,635	31.1%	33.7%
No	346	56.5%	57.5%	1892	73.2%	73.8%	11,091	61.2%	66.3%
N/A	10	1.6%		19	0.7%		1,392	7.7%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

Question (7):
"When you are finished with the Actiq unit, how are you disposing of it?"**

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 703)*	**% Of Responses** *(n = 703)*	**Totals**	**% Of Total** *(n = 2,791)*	**% Of Responses** *(n = 2,791)*	**Totals**	**% Of Total** *(n =18,822)*	**% Of Responses** *(n =18,822)*
Throw it in the trash	539	76.7%	76.7%	2404	86.1%	86.1%	12,871	68.4%	68.4%
Put under hot tap water and then in the trash	104	14.8%	14.8%	220	7.9%	7.9%	3,515	18.7%	18.7%
Using the safety container from the Welcome Kit	31	4.4%	4.4%	61	2.2%	2.2%	383	2.0%	2.0%
Cut the medicine off so that it falls into the toilet	2	0.3%	0.3%	8	0.3%	0.3%	133	0.7%	0.7%
Other	27	3.8%	3.8%	98	3.5%	3.5%	1,920	10.2%	10.2%
Totals:	703	100.0%	100.0%	2,791	100.0%	100.0%	18,822	100.0%	100.0%

Question (8):
"What do you do if you don't completely finish the unit?"**

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 914)*	**% Of Responses** *(n = 914)*	**Totals**	**% Of Total** *(n = 3,213)*	**% Of Responses** *(n = 3,213)*	**Totals**	**% Of Total** *(n = 19,106)*	**% Of Responses** *(n = 19,106)*
Throw it in the trash	357	39.1%	39.1%	830	25.8%	25.8%	4,106	21.5%	21.5%
Put under hot tap water and then in the trash	241	26.4%	26.4%	565	17.6%	17.6%	5,470	28.6%	28.6%
Using the safety container from the Welcome Kit	21	2.3%	2.3%	54	1.7%	1.7%	259	1.4%	1.4%
Cut the medicine off so that it fall into the toilet	7	0.8%	0.8%	44	1.4%	1.4%	306	1.6%	1.6%
(Always finish)	243	26.6%	26.6%	1525	47.5%	47.5%	3,357	17.6%	17.6%
Other or N/A	45	4.9%	4.9%	195	6.1%	6.1%	5,608	29.4%	29.4%
Totals:	914	100.0%	100.0%	3,213	100.0%	100.0%	19,106	100.0%	100.0%

Question (9):
"Starting dose"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 582)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 1,770)*	**Totals**	**% Of Total** *(n = 18,118)*	**% Of Respondents** *(n =15,001)*
200 mcg	159	26.0%	27.3%	314	12.2%	17.7%	2,932	16.2%	19.5%
400 mcg	200	32.7%	34.4%	711	27.5%	40.2%	6,843	37.8%	45.6%
600 mcg	84	13.7%	14.4%	290	11.2%	16.4%	2,227	12.3%	14.8%
800 mcg	109	17.8%	18.7%	364	14.1%	20.6%	2,406	13.3%	16.0%
1200 mcg	24	3.9%	4.1%	69	2.7%	3.9%	383	2.1%	2.6%
1600 mcg	6	1.0%	1.0%	22	0.9%	1.2%	210	1.2%	1.4%
N/A	30	4.9%		813	31.5%		3,117	17.2%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

Question (10):
"What dosage strength are you currently using?"

	Qtr 4			YTD Totals 2006			Cumulative Totals: *(Through Inception)*		
Response	**Totals**	**% Of Total** *(n = 612)*	**% Of Respondents** *(n = 607)*	**Totals**	**% Of Total** *(n = 2,583)*	**% Of Respondents** *(n = 2,576)*	**Totals**	**% Of Total** *(n = 18,118)*	**% Of Respondents** *(n =17,753)*
200 mcg	80	13.1%	13.2%	439	17.0%	17.0%	4,147	22.9%	23.4%
400 mcg	141	23.0%	23.2%	804	31.1%	31.2%	6,993	38.6%	39.4%
600 mcg	107	17.5%	17.6%	452	17.5%	17.5%	2,536	14.0%	14.3%
800 mcg	172	28.1%	28.3%	600	23.2%	23.3%	2,916	16.1%	16.4%
1200 mcg	63	10.3%	10.4%	178	6.9%	6.9%	708	3.9%	4.0%
1600 mcg	44	7.2%	7.2%	103	4.0%	4.0%	453	2.5%	2.6%
N/A	5	0.8%		7	0.3%		365	2.0%	
Totals:	612	100.0%	100.0%	2,583	100.0%	100.0%	18,118	100.0%	100.0%

****More than one choice may be selected**

Appendix 2

IMS National Disease and Therapeutic Index (NDTI)

Measure : P-Default Measure (Thousands)

	P-Drug Uses CalQtr/12/2006
ACTIQ CEH 99/04	18
RHEUMATOID ARTHRITIS	13
7229 DISC DISORDER OTH+UNS	4
7219 SPONDYLOSIS OF SPINE UNS	1
CANCER	---
MIGRAINE	---
NEUROLOGICAL	---
NEUROPATHIC PAIN	---
V670 POST OP SURGICAL EXAM	---
1629 MAL NEO BRONCH+LUNG UNSP	---
1729 MAL MEL SKIN UNSP SITE	---
1889 MAL NEO BLADDER	---
1890 MAL NEOPLASM KIDNEY	---
2848 OTHER APLASTIC ANEMIA	---
3462 VARIANTS OF MIGRAINE	---
3536 PHANTOM LIMB SYNDROME	---
4659 AC RESP INF UNSP SITE	---
7071 ULCER LOW LIMBS EXC DECU	---
7104 POLYMYOSITIS	---
7140 RHEUMATOID ARTHRITIS NEC	---
7230 CERVICAL SPINAL STENOSIS	---
7231 CERVICALGIA	---
7234 BRACH NEURITIS OR RADICU	---
7244 THOR LUMBOS NEUR RAD NEC	---
7288 DIS MUSC LIG+FASCIA OTH	---
7558 SPEC ANOM LIMB UNSP OTH	---
7809 CHRONIC PAIN SYNDROME	---
8230 FR TIB+FIB UP OR UNS CL	---

Appendix 3

This table provides a comprehensive tabulation of *Actiq* Product Experience Reports to date (i.e., for the period covering April/May 1999 through 31-December-2006). Also included are any cases involving serious Adverse Drug Experiences (ADEs) and/or off-label usage.

Month/Yr	Total No. of Cases[§]	Off-Label Inquiry	Off-Label Prescribing	SAE Related to Diversion or Off-Label Use	Pediatric Related	SAE On-Label Use
April/May 1999	3	1*	2**	0	0	0
June 1999	3	1*	0	0	0	2
July 1999	1	0	1**	0	0	0
August 1999	1	0	1***	0	0	0
September 1999	1	0	0	0	0	1
October 1999	2	0	1***	0	0	1
November 1999	4	0	1**	0	0	3
December 1999	6	0	2***	0	0	4
January 2000	0	0	0	0	0	0
February 2000	1	0	1**	0	0	0
March 2000	6	0	3** 1***	0	0	2
April 2000	10	0	4** 3***	0	0	3
May 2000	7	0	3** 2***	0	0	2
June 2000	1	0	1***	0	0	0
July 2000	9	1** 1***	1** 1***	0	0	5
August 2000	5	0	1** 1***	0	1	2
September 2000	6	0	2**	0	0	4
October 2000	5[§]	0	2**	1	0	1
November 2000	2[§]	0	0	0	0	1
December 2000	8[§]	0	0	0	1	6
January 2001	4[§]	0	2*** 1**	0	0	1
February 2001	3[§]	0	3**	0	0	0
March 2001	7[§]	0	2*** 5**	0	0	0
April 2001	8	0	2*** 2**	0	0	1 1†

Month/Yr	Total No. of Cases§	Off-Label Inquiry	Off-Label Prescribing	SAE Related to Diversion or Off-Label Use	Pediatric Related	SAE On-Label Use
May 2001	9	0	2** 4***	0	0	1 1†
June 2001	10	0	1*** 7**	1	1	0
July 2001	10	0	8** 0***	0	0	0
August 2001	11	0	7** 2***	1	0	0
September 2001	11	0	5** 1***	1	0	0
October 2001	8	0	3** 2***	1	1	1
November 2001	6	0	3** 1***	0	0	0
December 2001	7	0	1** 2***	0	0	1
January 2002	31	1	20** 5***	2	2	1
February 2002	23	0	5** 5***	0	1	4
March 2002	23	0	10** 3***	0	1	1
April 2002	27	1	20** 2***	0	1	3
May 2002	32	0	12** 9***	0	1	2
Jun 2002	26	1	12** 6***	0	1	0
July 2002	39	0	19** 12***	4	1	2
August 2002	42	0	21** 15***	0	0	1
September 2002	40	1	16** 14***	1	1	1
October 2002	45	0	21** 13***	1	0	3
November 2002	28	0	14** 9***	1	1	1
December 2002	36	0	17** 12***	4	0	0
January 2003	36	0	22** 10***	1	0	0
February 2003	50	0	29** 11***	0	2	0

Month/Yr	Total No. of Cases§	Off-Label Inquiry	Off-Label Prescribing	SAE Related to Diversion or Off-Label Use	Pediatric Related	SAE On-Label Use
March 2003	45	0	16** 23***	2	3	0
April 2003	40	0	16** 15***	1	2	0
May 2003	49	2	24** 21***	3	2	0
June 2003	44	3	24** 17***	2	0	0
July 2003	196	5	112** 84***	0	0	1
August 2003	617	5	297** 319***	2	0	1
September 2003	330	0	155** 175***	1	3	0
October 2003	171	2	72** 99***	2	1	1
November 2003	96	4	47** 49***	5	1	0
December 2003	63	3	35** 28***	1	0	2
January 2004	66	1	36** 30***	2	0	1
February 2004	61	1	33** 27***	2	0	0
March 2004	57	2	35** 20***	1	0	0
April 2004	77	2	20** 57***	1	3	3
May 2004	73	4	25** 48***	2	1	0
June 2004	61	3	20** 41***	1	0	0
July 2004	85	2	25** 30*** 22****	2	0	1
August 2004	63	1	27** 24*** 10****	0	0	1
September 2004	93	3	30** 35*** 18****	0	4	0
October 2004	86	3	29** 33*** 18****	4	3	2

Month/Yr	Total No. of Cases§	Off-Label Inquiry	Off-Label Prescribing	SAE Related to Diversion or Off-Label Use	Pediatric Related	SAE On-Label Use
November 2004	56	0	18** 21*** 8****	1	2	0
December 2004	78	2	31** 28*** †8****	4	2	0
January 2005	130	3	47** 43*** 39****	4	1	1
February 2005	93	2	38** 38*** 17****	1	0	0
March 2005	167	3	51** 48*** 52****	3	11	3
April 2005	239	included under off-label prescribing	72** 113*** 52****	1	0	2
May 2005	224	included under off-label prescribing	67** 100*** 53****	2	2	0
June 2005	187	included under off-label prescribing	52** 65*** 64****	2	3	8
July 2005	192	included under off-label prescribing	50** 75*** 63****	0	3	2
August 2005	200	included under off-label prescribing	48** 81*** 66****	3	2	1
September 2005	170	included under off-label prescribing	49** 70*** 47****	2	1	0
October 2005	197	included under off-label prescribing	57** 69*** 63****	2	4	0
November 2005	129	N/A	35** 41*** 52****	0	1	1
December 2005	116	N/A	27** 50*** 35****	2	1	2

N/A: Included under off-label prescribing, where applicable.
* Pharmacist did not dispense drug because of potential off-label use.
** Appropriate physician follow-up letter scheduled or sent.
*** Physician's name was not revealed; therefore, follow-up letter could not be sent.
****Repeat incident notification scheduled or sent.
§Not included are non-serious, on-label ADEs. Non-Human exposures are no longer classified as product experience reports
ǂ Solicited reports from a Phase 4 trial in progress.
† In addition, there was one additional repeat incident notification sent following receipt of follow-up information for a case received in a prior quarter.

Month, 2006	Total No. of RMP Cases	Off-Label Prescribing	SAE Related to Off-Label/On-Label[§] Use	Unintended Pediatric Exposure	Diversion SAE/No SAE
January 2006	152	45** 47*** 58****	2/0	1	1/1*
February 2006	201	56** 56*** 89****	0/1	0	0/1*
March 2006	274	61** 62*** 121****	1/5	28	0/2
April 2006	225	61** 49*** 113****	1/1	1	0/2
May 2006	191	63** 45*** 78****	2/0	3	0/2
June 2006	160	58** 24*** 72****	3/0	0	1/2
July 2006	192	47** 29*** 114****	0/1	1	1/1
August 2006	271	88** 37*** 140****	1/0	1	0/3
September 2006	165	50** 42*** 71****	0/0	0	0/1
October 2006	267	73** 58*** 128****	2/0	0	1/5
November 2006	159	46** 34*** 74****	1/0	2	0/5
December 2006	101	25** 22*** 52****	1/0	0	1/1

N/A: Included under off-label prescribing, where applicable.
* Pharmacist did not dispense drug because of potential off-label use.
** Appropriate physician follow-up letter scheduled or sent.
*** Physician's name was not revealed; therefore, follow-up letter could not be sent.